Antimicrobial resistance: opportunity for Europe to establish global leadership

Published Online December 18, 2015 http://dx.doi.org/10.1016/S1473-3099(15)00410-7

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Antimicrobial resistance heightens the prospect of readily curable infections becoming pathogens with pandemic potential. Although in high-income settings progress has been made to curb the rise of resistance,[1] the scarcity of new antimicrobial drugs remains a challenge.

The Independent Review on Antimicrobial Resistance, launched in 2014, estimated a population reduction by 2050 of between 11 million and 444 million people in a world without effective antibiotics, and a reduction in the size of the global economy by 0·1–3·1%.[2] The US Centers for Disease Control and Prevention estimates the direct costs of antimicrobial resistance at US$20 billion, with additional productivity losses of $35 billion.[3] In Europe, historical estimates from 2009 suggest a direct and indirect cost of €1·5 billion.[4] Notwithstanding the large discrepancies in these estimates and the wide uncertainties, the health, economic, and societal risks of antimicrobial resistance are simply too great to be ignored.

Sometimes difficult to conceive in view of their ubiquity in health care, antibiotics have only been used routinely over the past 75 years. In that time, antibiotics have instrumentally shaped the quality of medicine and clinical practice that we see today. Beyond health care, antibiotics are widely used in the human food system, agriculture, and aquaculture.[5] Existing strategies to address antimicrobial resistance focus on antibiotic prescriptions for human beings (both appropriate and inappropriate) and consumption by livestock. Regulation of livestock consumption is particularly challenging—in China and India alone, antibiotic consumption by livestock is expected to rise from more than 15 000 tonnes in 2010 to 40 000 tonnes in 2030.[5] Whether effective mechanisms and policies can be implemented to ensure appropriate antibiotic use in livestock remains to be seen. The principle of one health will therefore be central to any progress in curbing antimicrobial resistance.

Increasingly better quality data exist on the patterns of emerging antimicrobial resistance and of antibiotic usage. Europe has had success in reducing antimicrobial resistance, as documented by the European Antimicrobial Resistance Surveillance Network.[6] For example, cases of meticillin-resistant *Staphylococcus aureus* across hospitals in several countries have decreased each year after the introduction of infection control practices and local hospital guidelines. The level of success varies, however, across the 50 countries of the WHO European Region.[4,6]

Ruth Kelly and colleagues[7] report new data to map the landscape and pattern of investment in antibacterial resistance research. Data from the European Union and the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) are included, incorporating public funding for research across 17 European countries, Canada, and Israel. The findings are revealing; between 2007 and 2013, €1·3 billion of research investment came from public sources, with two-thirds of funding earmarked for novel therapeutics, but only €12·5 million of that funding was dedicated to the environment and €25·1 million to surveillance. A further mismatch shown by the study is the substantial variability of national-level studies; the UK accounted for almost 500 of the 1208 nationally funded studies, with Canada, the second largest contributor, coordinating about 100 studies during the same period.

The results of the study by Kelly and colleagues[7] emphasise both the shortcomings of and hope for antimicrobial research funding. However, with concerted leadership, all states in the JPIAMR network and beyond should be able to reinforce their partnership, share best practices, and change the course of the status quo. The UK's leadership to prioritise antimicrobial resistance as an important global challenge is translating into tangible action,[8,9] but the strategy has room for improvement. A coordinated, global effort combining drug resistance, antibiotic pipeline, antibiotic usage, and investment data is urgently needed. Kelly and colleagues build on the published literature[10,11] and provide a basis for harmonisation to begin—at the very least on a European platform.

As with any research programme, the quality and completeness of data are essential, and for these analyses to be complete, a real partnership needs to exist between public, philanthropic, and private funders. These partnerships are particularly important for antimicrobial resistance because of market failure,[12] the dependence on the pharmaceutical industry to deliver novel therapeutic drugs, and the social imperative to

allocate limited resources responsibly with a sense of urgency. Furthermore, research and surveillance needs to be expanded beyond Europe, the USA, and Canada for antimicrobial resistance to be adequately controlled. With antibiotic sales data predicting influenza-like illness in the USA,[13] early point-of-care diagnostics for overlapping clinical syndromes should be a priority area, particularly in low-income and middle-income settings.

The global scientific and health policy communities must rise to the challenge of antimicrobial resistance (and opportunity) to develop resilient health systems for effectively managing resistance, redistribute collaborative research studies, and realign investments across countries. The human and economic cost of playing catch up is simply too great a risk to bear.

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We declare no competing interests.

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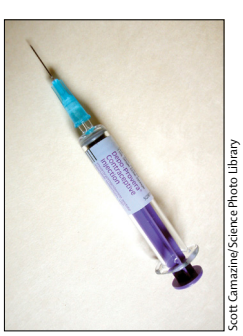
The role of progestins in HIV acquisition in young women

In *The Lancet Infectious Diseases*, Elizabeth Byrne and colleagues[1] report the biological mechanism by which injectable progestin-only contraceptives, such as depot medroxyprogesterone acetate (DMPA) and norethindrone enanthate (NET-EN), or endogenous progesterone might act to increase the risk of HIV acquisition in women. They report that HIV-negative injectable progestin-only contraceptive users had a 3·92 times higher frequency of cervical HIV target cells than women using no long-term contraceptive (p=0·0241), and women using no long-term contraceptive in the luteal phase of the menstrual cycle (a naturally high-progestin state) also had a 3·25 times higher frequency of cervical target cells than those in the lower-progestin follicular phase (p=0·0488).

The role of injectable progestin-only contraceptives as a risk factor for HIV acquisition has been debated for several years.[2] Although this question has not been addressed in adequately powered randomised controlled trials, several secondary analyses[3,4] of large randomised controlled trials have estimated an increased risk for injectable progestin-only contraceptives, some of which are able to distinguish between DMPA and NET-EN. An individual patient data analysis[5] reported a significant increase in HIV incidence in women using DMPA, and a non-significant increase in this direction for NET-EN.

WHO convened a special meeting in 2012 to discuss the evidence available at the time, resulting in the release of a technical statement.[6] WHO recommended that women receiving injectable progestin-only contraceptives should use other HIV prevention methods such as male and female condoms in conjunction to prevent HIV acquisition. The panel also recommend that, first, further consideration should be given to high quality research designs to confirm the role of progestin hormonal contraception in HIV acquisition;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Published Online
December 23, 2015
http://dx.doi.org/10.1016/S1473-3099(15)00476-4

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